Enantioselective Synthesis of Protected Isotetronic Acids

Dieter Enders,* Hubert Dyker, and Frederik R. Leusink

Dedicated to Professor Waldemar Adam on the occasion of his 60th birthday

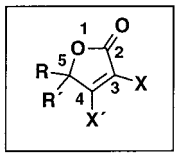
Abstract: Isotetronic acids are subunits of a number of natural products. They are of interest in agricultural and pharmaceutical research and are important synthetic intermediates. This paper describes the first highly diastereo- and enantioselective synthesis of isotetronic acids in 4 to 5 steps (*de*, *ee* > 98 %). Key steps in the reaction sequence are the diastereoselective aldol reaction of the 2-oxoesters **5** as their SAEP hydrazones (*S*)-**6** with aldehydes, followed by base-promoted lactonization to the hydrazonolactones **8.** Subsequent oxidative cleavage of the hydrazone moiety afforded the enantiomerically pure *O*-protected isotetronic acids (*R*)-/(*S*)-**9**.

Keywords: aldol reactions · asymmetric synthesis · hydrazones · isotetronic acids · pyruvate

Introduction

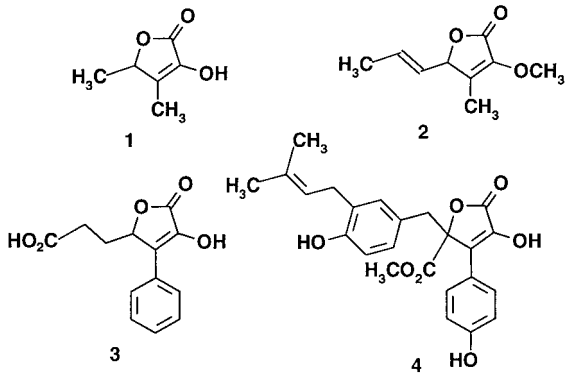
Tetronic acids and isotetronic acids are frequently found in nature and have been isolated from a variety of natural sources. Due to the wide range of its biological activity, this class of compounds has received considerable attention in agricultural and pharmaceutical research. The common structural feature of these compounds is the central 2-(5H)-furanone unit **A**, substituted with hydroxy or alkoxy groups at position 3 or 4. To our knowledge, the bis-substituted functionality of **A**, with hydroxy groups at both the 3- and 4-positions, occurs only in vitamin C (L-ascorbic acid) and in the macrolide antibiotic chlorothricin.[1] Importantly, in this class of compounds the synthetic 4-(4-chlorophenyl)-2-hydroxytetronic acid (CHTA)[2a, b] and the recently reported enantiomerically pure 4-aryl-2-hydroxytetronic acids[2c] have been shown to be potent inhibitors of platelet aggregation as well as inhibitors of cyclooxygenase and 5-lipoxygenase.

Isotetronic acids, the subject of this work, have been isolated from a number of different natural sources and are of major interest as valuable building blocks.[3–9] Four examples of naturally occurring isotetronic acids may demonstrate the importance of this class of compounds.



X, X´ = H, C, OH, OR

A



Sotolon (**1**)[5] is a very important volatile aroma component isolated from raw sugarcane, botrytized wine, flor sherry, and a variety of foods, and is also found in roasted tobacco volatiles. It has been identified only in its racemic form.

Serpenone (**2**)[6] was isolated as a metabolite of the higher fungus *Hypoxylon serpens*. Serpenone and synthetic analogues are potentially useful for the treatment of diabetic neuropathy. WF-3681 (**3**), another fungal metabolite, was isolated from *Chaetomella raphigera*. It has been reported to have aldose reductase inhibitory activity.[7] Recently, a Japanese group reported the isolation of the more complex isotetronic acid **4** from the fungi *Aspergillus terreum* and

[*] Prof. Dr. D. Enders, Dr. F. R. Leusink
Institut für Organische Chemie der Technischen Hochschule
Professor-Pirlet-Str. 1, D-52074 Aachen (Germany)
Fax: Int. code +(49) 241 8888-127
E-mail: enders@rwth-aachen.de
Dr. H. Dyker
Bayer AG, Zentrale Forschung, Geb. Q18
D-51368 Leverkusen (Germany)
Fax: Int. code +(49) 214 30-56656
E-mail: hubert.dyker.hd@bayer-ag.de

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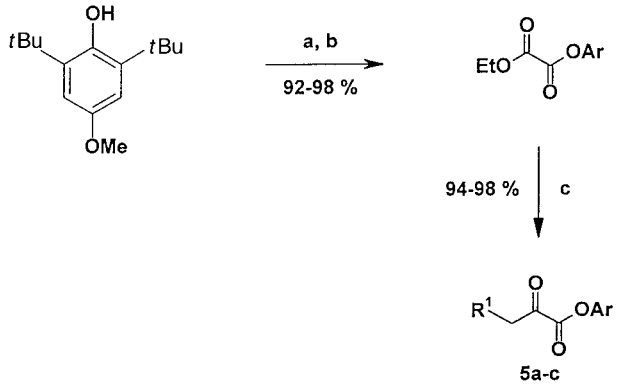
demonstrated that **4** exhibits promising antitumor activity in mice FM3A tumor cells.[8]

Although there are numerous reports in the literature on the synthesis of racemic mixtures of isotetronic acids, the synthesis of enantiomerically pure isotetronic acids[9] is based on the vast array of naturally occurring building blocks (ex-chiral-pool synthesis) such as carbohydrates,[9] ascorbic acid,[9] hydroxycarboxylic acids,[5e] and hydroxyamino acids.[5g] An attempt to synthesize sotolon by means of a chemoenzymatically assisted reaction starting from a racemic precursor gave virtually racemic material.[5]

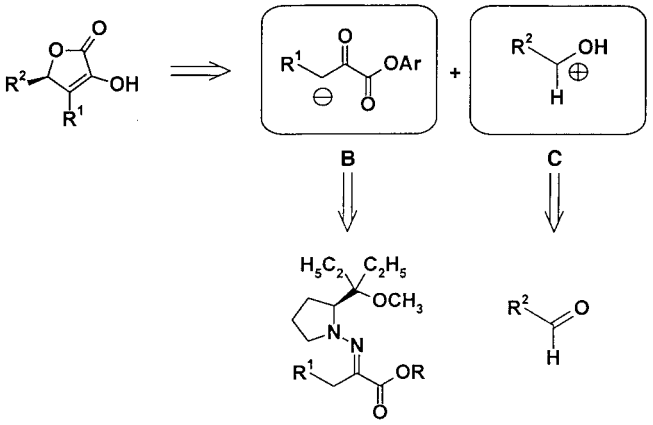
Here we report a highly enantioselective and flexible approach to isotetronic acids by an asymmetric synthesis based on our well-established hydrazone methodology.



Scheme 2. Synthesis of the 2-oxoester **5**. R^1 = H, Me, Ph; Ar = 2,6-di-*tert*-butyl-4-methoxyphenyl. Reagents and conditions: a) *n*BuLi, THF, 0 °C; b) EtO_2COCl; c) R^1CH_2MgBr, Et_2O, −78 °C.

Results and Discussion

The retrosynthetic analysis of isotetronic acids by cleavage of the lactone functionality and of the C-3/C-4 bond leads to the anionic d^2-synthon **B** and the cationic synthon **C** (Scheme 1).

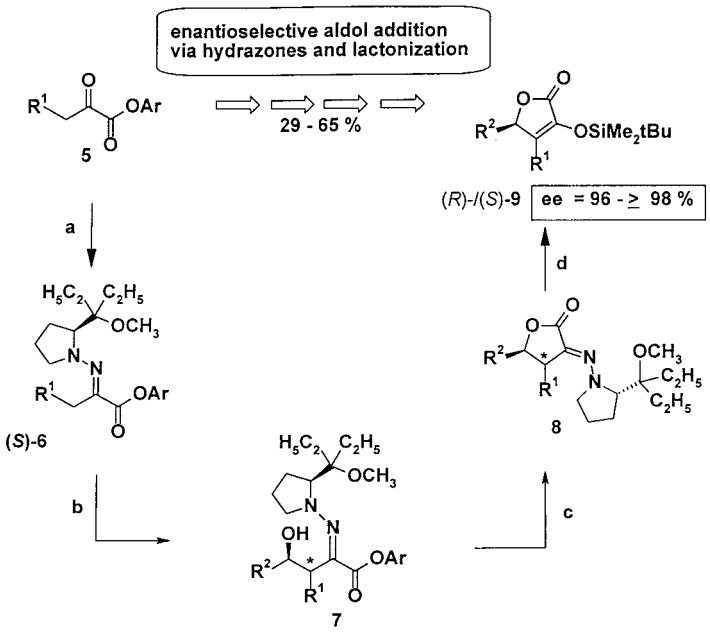


Scheme 1. Retrosynthetic analysis of isotetronic acids.

Stereoselective aldol reaction of the corresponding azaenolate of synthon **B** with aldehydes promoted by the chiral auxiliary, and subsequent lactonization and functional group manipulation of the hydrazone unit, would then permit access to the isotetronic acids.

Imitation of the synthetic principle used by nature for the biosynthesis of ulosonic and sialic acids led us to a chemical equivalent for phosphoenol pyruvate (PEP) and its homologues, which we recently reported[10] and which serves as anionic synthon **B**.

The *O*-silyl-protected isotetronic acids **9** have been synthesized efficiently in a four- to five-step sequence starting from the 2-oxocarboxylic esters **5** with a sterically blocked ester functionality (Schemes 2 and 3). Key steps are the diastereoselective aldol reaction of the hydrazones (*S*)-**6** with aldehydes and subsequent lactonization. As depicted in Scheme 2, the starting 2-oxoesters **5** were readily prepared in excellent yields on a large scale by a simple two-step process: esterification of ethyl oxalyl chloride with the lithium



Scheme 3. Enantioselective synthesis of *O*-*t*$BuMe_2$Si-protected isotetronic acids (*S*)-/(*R*)-**9** by asymmetric aldol reaction of 2-oxocarboxylic esters **5** via the SAEP hydrazone (*S*)-**6** (Ar = 2,6-di-*tert*-butyl-4-methoxyphenyl; for substituents R^1 and R^2 see Table 1.). Reagents and conditions: a) SAEP, *c*-hexane, reflux, 75–83 %. For (*S*)-**6a** (R = H): b) i) LDA, LiBr, THF, −78 °C; ii) RCHO, −90 °C → −78 °C; iii) saturated NH_4F solution; c) *t*BuLi or *t*BuOK, THF, −78 °C → −10 °C; d) i) O_3, CH_2Cl_2, −78 °C; ii) *t*$BuMe_2$SiCl, imidazole, CH_2Cl_2. For (*S*)-**6b,c** (R = Me, Ph): b/c) i) LDA, LiBr, THF/DMPU (30–50 %), −78 °C; ii) RCHO, −90 °C → −10 °C, iii) saturated NH_4F solution; d) as described above.

salt of 2,6-di-*tert*-butyl-4-methoxyphenol, followed by chemoselective addition of Grignard reagents to the unsymmetrical oxalic acid ester at low temperatures furnished the desired 2-oxoesters **5a–c** in excellent yield (86–96 % overall in 2 steps).

The chiral auxiliary is then introduced in the first step of the asymmetric reaction sequence by condensation of the 2-oxoesters **5a–c** with the chiral hydrazine (*S*)-1-amino-2-(1-ethyl-1-methoxypropyl)pyrrolidine (SAEP).[11] The hydrazones were obtained exclusively as *E* isomers in the form of pale yellow oils [(*S*)-**6a,b**: 83 %, (*S*)-**6c**: 75 %]. In order to

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achieve high diastereoselectivities in the aldol step, we found it necessary to introduce the sterically more demanding auxiliary SAEP instead of SAMP.[10b] Depending on the hydrazones (*S*)-**6a** (R^1 = H) or (*S*)-**6b**/**6c** (R^1 = Me, Ph) the metalation conditions had to be modified and optimized. In the case of the hydrazone of pyruvic acid ester ((*S*)-**6a**), complete formation of the azaenolate was possible when LDA was used as base in the presence of one equivalent of lithium bromide in THF.[10b,c, 12] The base is readily prepared by treating diisopropylamine hydrobromide with two equivalents of *n*-butyllithium. Self-condensation of the highly reactive azaenolate ester was prevented by sterically blocking the ester reactivity as the 2,6-di-*tert*-butyl-4-methoxyphenyl ester.[10a–c] Reaction of the metalated hydrazone with a variety of aldehydes at −90 °C furnished the aldol products (*S,R*)-/(*S,S*)-**7a–e** in a clean reaction (Table 1). The products were isolated by flash chromatography and obtained in excellent yields with high diastereomeric excesses (84–96 %, *de* = 88–98 %). Only in the case of the protected (*R*)-*O*-cyclohexylidene glyceraldehyde was the aldol product (*S,S,R*)-**7e** isolated in significantly lower yield. In this case, the hydrazonolactone (*S,S,R*)-**8e** was isolated, along with the aldol product, owing to rapid lactonization of the intermediate lithium alkoxide ester [47 % (*S,S,R*)-**7e** and 45 % (*S,S,R*)-**10e**, *de* > 98 %]. It is remarkable that virtually complete asymmetric induction was obtained with a methyl ketone as methylene component in a stereochemical situation which is difficult to control in aldol and aldol-type reactions.[13]

After some experimentation, we found that lactonization of the aldol products **7** and concomitant removal of the ester-protecting group is best achieved by treating **7** with *tert*-butyl lithium or potassium *tert*-butoxide in THF at low temperature. After flash chromatography, the hydrazonolactones (*S,R*)-/(*S,S*)-**8a–e** were obtained diastereomerically pure in good to excellent yields (72–92 %, *de* > 98 %). The protecting group, 2,6-di-*tert*-butyl-4-methoxyphenol, can be recycled. The metalation and aldol addition of the homologous hydrazones (*S*)-**6b,c** (R^1 = Me, Ph) required the addition of the cosolvent *N,N′*-dimethylpropylurea (DMPU, 30–50 %) to the base LDA/LiBr. The metalation as described above without cosolvent or the use of the complex Lochmann–Schlosser base (*t*BuOK/*n*BuLi), which worked well for the alkylation of the homologous hydrazones,[10a] proved unsuccessful in this case. These three reactions (metalation/aldol addition/cyclization) can also be performed as a tandem reaction to the desired hydrazonolactones **8f–h** without prior isolation of the aldol product. In this case, the reaction mixture is simply warmed to −10 °C after addition of the aldehyde. The intermediate lithium alkoxide ester cyclizes under these conditions to the hydrazonolactones **8f–h**. The hydrazones **8f** and **8g** were obtained as a diastereomeric mixture (*S,S,S*)/(*S,R,S*) and used as such in the subsequent reaction (**8f**: diastereomeric ratio = 21:1, **8h**: diastereomeric ratio = 4:3). NMR spectroscopic analysis revealed that the newly formed stereogenic center at the hydroxy group was fully induced. Since the cleavage of the hydrazone moiety would remove the C-2 center by tautomerism, the moderate diastereoselectivities did not present a problem. In the case of the hydrazone **8h**, the diastereomers (*S,R,R*) and (*S,S,R*) were separated from the (*S,S,S*)-isomer in 63 % yield by simple flash chromatography before further reaction (diastereomeric ratio = 10:2.6:1).

Cleavage of the hydrazones in the last step of the reaction sequence was best achieved by ozonolysis at low temperature. However, it was difficult to isolate the pure isotetronic acids without protection of the hydroxy group. The *tert*-butyldimethylsilyl group proved to be the most effective protecting group. The silyl group was introduced under standard

Table 1. Highly enantiomerically enriched isotetronic acids (*S*)-/(*R*)-**9** synthesized by enantioselective aldol addition and lactonization from the 2-oxoesters **5** via the SAEP hydrazones (*S*)-**6**.

7/8/9	R^1	R^2	Yield 7 [%]	*de* 7 [%][a]	Yield 8 [%]	*de* 8 [%][a]	Yield 9 [%]	*ee* [%][a]	$[\alpha]_D^{23}$ (*c*, $CHCl_3$)	Config.
a	H	Bu	84	93	87	≥98	72	≥98	-8.0 (0.85)	(*R*)
b	H	*i*Bu	94	88	80	≥98	58	≥98	-2.0 (0.98)	(*R*)
c	H	4-MePh	96	≥98	72	≥98	81	≥98	-31.6 (1.04)	(*S*)
d	H	Ph	86	≥98	72	≥98	83	98.4[c]	-38.4 (0.91)	(*S*)
e	H		47[d]	≥98	92	≥98	77	≥98	-47.5 (0.94)	(*S,R*)
f	Me	4-MePh	n.d.	n.d.	54	91[e]	65	96[f]	-88.8 (0.97)	(*R*)
g	Ph	4-MePh	n.d.	n.d.	88	14[e]	65	98[f]	-43.3 (1.04)	(*R*)
h	Ph	*i*Bu	n.d.	n.d.	63	50[e]	72	≥96	-36.8 (0.95)	(*R*)

[a] Determined by ^{13}C NMR spectroscopy. [b] Based on the *de* of hydrazones **8** determined by ^{13}C NMR spectroscopy. [c] Determined by GC on a chiral cyclodextrin phase. [d] Along with the aldol product **7e**, 45 % of **10e** was isolated. [e] Diastereomeric ratios by NMR: **8f**: (*S,S,S*)/(*S,R,S*) = 21:1, **8g**: (*S,S,S*)/(*S,R,S*) = 4:3, **8h**: yield for the (*S,R,R*)/(*S,S,R*)-mixture (*S,R,R*)/(*S,S,R*)/(*S,S,S*) = 10:2.6:1. [f] Determined by Pirkle shift experiments. n.d. = not determined.

conditions (tBuMe$_2$SiCl, imidazole, CH_2Cl_2) and without racemization in a one-pot reaction immediately after ozonolysis and allowed the isolation of the final products (*R*)-/(*S*)-**9**. Protection with the acetyl function (Ac_2O, NEt_3, or DMAP) caused epimerization at the aldol center.

The values given for the enantiomeric excesses of the products (*R*)-/(*S*)-**9** refer to the diastereomeric excesses of the hydrazones **8**, which were determined by ^{1}H and ^{13}C NMR spectroscopy. The enantiomeric excess of (*R*)-**9d** was determined to be *ee* = 98.4 % by capillary gas chromatography on a chiral cyclodextrin phase. This value is in accordance with the diastereomeric excess of the corresponding hydrazone (*S*,*R*)-**8d** (*de* = 98 %), and thus proves that the introduction of the *O*-protecting group and the subsequent cleavage of the hydrazone proceed without racemization. The enantiomeric excesses of **9f** und **9g** were determined by NMR spectroscopy from Pirkle shift experiments with (−)-(*R*)-(9-anthranyl)-2,2,2-trifluoroethanol (*ee* = 96 % and *ee* = 98 %).

The stereochemical assignments given in the schemes and in the table are based on the X-ray crystal structure analysis of the aldol product (*S*,*R*)-**7b** with the hydroxy function protected by a benzyloxymethyl(BOM) group (Figure 1).[15] A

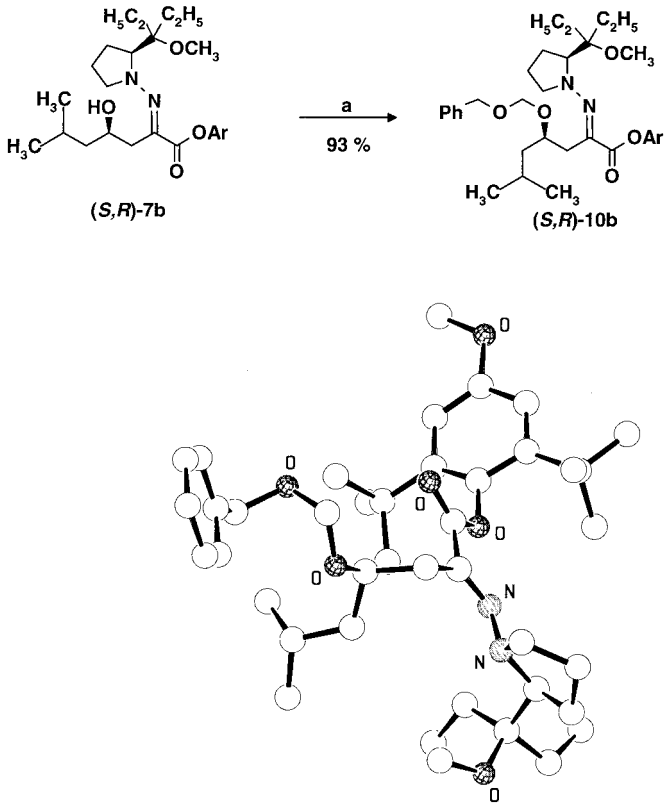

Figure 1. Synthesis of (*S*,*R*)-**10b** and the X-ray structure of one of the two independent molecules of (*S*,*R*)-**10b** (Schakal plot). Ar = 2,6-di-*tert*-butyl-4-methoxyphenyl. Reagents and conditions: a) $PhCH_2OCH_2Cl$, iPr$_2$NEt, nBu$_4$NI, CH_2Cl_2, reflux 15 h.

similar reaction mechanism for the chiral PEP equivalent and its homologues is assumed. The BOM group was introduced by reaction of the aldol product with excess benzyloxymethylchloride in the presence of Hünig's base to give (*S*,*R*)-**10b** (93 %). The crystal structure analysis proved unambigously a (*R*)-configuration at the newly generated stereogenic aldol center. This result is in agreement with previous results observed by our research group for aldol reactions with SAMP/RAMP hydrazones.[14]

Conclusion

The method described in this paper for the synthesis of protected, highly enantiomerically enriched isotetronic acids is, to our knowledge, the first asymmetric synthesis of this interesting class of compounds. By choosing different aldehydes and 2-oxocarboxylic esters as starting materials, it is possible to introduce a wide range of substituents for R^1 and R^2. The isotetronic acids described here should be of interest as chiral intermediates and as biologically active compounds.

Experimental Section

General: Solvents were dried immediately prior to use. Dry tetrahydrofuran (THF) was distilled from potassium/benzophenone under Ar. Dichloromethane and Hünig's base (iPr$_2$NEt) were distilled from CaH_2 and stored under Ar. Ether and petroleum ether were distilled prior to use. All reactions were monitored by thin-layer chromatography (tlc) carried out on analytical silica gel tlc plates purchased from Merck (Darmstadt) and visualized with UV light, 7 % ethanolic phosphomolybdic acid, and heat. Commercial reagents were used directly as received. All reactions were carried out under anhydrous conditions under Ar, unless otherwise stated. Yields refer to chromatographically and spectroscopically homogenous materials.

Optical rotations were measured on a Perkin – Elmer P241 polarimeter and with solvents of UVASOL quality (Merck). Microanalyses were obtained with a CHN-O-RAPID elemental analyser. ^{1}H and ^{13}C NMR spectra were recorded on a Varian VXR300, Gemini300 (300 and 75 MHz) or Varian Unity500 (500 and 125 MHz) with TMS as the internal standard. IR spectra of evaporated films were recorded on a Beckman Acculab4 and a Perkin – Elmer FT/IR spectrophotometer. Mass spectra were obtained on a Varian MAT212, EI 70 eV (relative intensities in parentheses). High-resolution mass spectra were recorded on a Finnigan MAT95. Melting points were measured on a Büchi apparatus and are uncorrected.

SAEP hydrazones (*S*)-6; general procedure: A solution of the 2-oxoester **5**, 1.1 equiv SAEP and 5 mol % *p*-toluenesulfonic acid in *c*-hexane (2 mL mmol^{-1}) were heated under reflux in a Dean – Stark trap until tlc indicated complete reaction. The solvent was removed in vacuo and the residue dissolved in ethyl acetate. The solution was washed with a saturated sodium chloride solution, dried over $MgSO_4$, and concentrated in vacuo. The hydrazones (*S*)-**6** were purified by flash chromatography (silica gel, petroleum ether/diethyl ether) and were obtained as highly viscous yellow oils.

(*S*)-(+)-1-[1-(2,6-Di-*tert*-butyl-4-methoxy-1-phenoxycarbonyl)-1-ethylideneamino]-2-(1-methoxy-1-ethylpropyl)pyrrolidine ((*S*)-6a): According to the general procedure, 2,6-di-*tert*-butyl-4-methoxyphenyl 2-oxopropionate [(*S*)-**5a**, 7.66 g, 25.0 mmol] was reacted with SAEP (5.03 g, 27 mmol) in cyclohexane for 20 h. After work-up, purification of the crude product by flash column chromatography (silica gel, petroleum ether/ether 4:1) afforded the hydrazone (*S*)-**6a** as a pale yellow viscous oil (9.90 g, 83 %); $[\alpha]_D^{23} = +844.3$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.85$, 0.89 (t, 2 × 3H; $C(CH_2CH_3)_2$), 1.60, 1.64 (s, 18H; 2C$(CH_3)_3$), 1.40 – 2.08 (m, 8H; $C(CH_2CH_3)_2$, $NCH_2CH_2CH_2$), 2.18 (s, 3H, CH_3C=N), 3.02 (m, 1H; NC*H*H), 3.31 (s, 3H; OCH_3), 3.71 (m, 1H; NCH*H*), 3.79 (m, 1H; $ArOCH_3$), 3.98 (m, 1H; NCH), 6.86 (m, 2H; 2arom H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 7.95$, 8.16 ($C(CH_2CH_3)_2$), 16.72 (CH_3C=N), 23.49 ($NCHCH_2$), 24.10, 25.22 ($C(CH_2CH_3)_2$), 26.96 (NCH_2CH_2), 31.23, 31.42 (2C$(CH_3)_3$), 35.60, 35.64 (2$C(CH_3)_3$), 50.41 ($ArOCH_3$), 56.90 (NCH_2),

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72.66 (NCH), 80.14 ($C(CH_2CH_3)_2$), 111.45, 111.53 (2 arom CH), 136.57 (CO_2Ar); IR (film): $\tilde{\nu}$ = 2966, 2879, 2831, 1719, 1589, 1456, 1449, 1431, 1420, 1365, 1300, 1252, 1219, 1187, 1143, 1099, 1066 cm^{-1}; $C_{28}H_{46}N_2O_4$ (474.7): calcd. C 70.85, H 9.77, N 5.90; found C 70.80, 9.81, N 6.08.

(*S*)-(+)-1-[1-(2,6-Di-*tert*-butyl-4-methoxy-1-phenoxycarbonyl)-1-propylideneamino]-2-(1-methoxy-1-ethylpropyl)pyrrolidine ((*S*)-6b): According to the general procedure, 2,6-di-*tert*-butyl-4-methoxyphenyl 2-oxobutyrate [(*S*)-**5b**, 9.60 g, 30 mmol] and SAEP (5.7 g, 31 mmol) were reacted in cyclohexane for 20 h. After work-up, purification of the crude product by flash column chromatography (silica gel, petroleum ether/ether 5:1) afforded the hydrazone (*S*)-**6b** as a pale yellow viscous oil (12.15 g, 83 %); $[\alpha]_D^{23} = +696.6$ (c = 1.07, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84, 0.89 (t, J = 7.5 Hz, 6H; $C(CH_2CH_3)_2$), 1.16 (t, J = 7.1 Hz, 3H; C=NCH_2CH_3), 1.32, 1.35 (s, 18H; $2C(CH_3)_3$), 1.50–2.05 (m, 8H; CH_2CH_2, $2CH_2CH_3$), 2.56 (qt, J = 7.1 Hz, J = 7.5 Hz; 1H), 2.71 (qt, J = 7.1 Hz, J = 7.5 Hz; 1H), 3.05–3.12 (m, 1H; $NCHHCH_2$), 3.28 (s, 3H; OCH_3), 3.70–3.78 (m, 1H; $NCHHCH_2$), 3.80 (s, 3H; $ArOCH_3$), 3.92–3.98 (m, 1H; $NCHCH_2$), 6.86, 6.88 (d, J = 3 Hz, 1H; 2 arom CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.93, 8.20 ($2CH_2CH_3$), 12.31 (CH_3CH_2C=N), 22.68 (CH_2C=N), 23.51, 24.05 ($C(CH_2CH_3)_2$), 25.21 ($NCHCH_2$), 26.88 (NCH_2CH_2), 31.13, 31.48 ($C(CH_3)_3$), 35.57, 35.66 ($C(CH_3)_3$), 50.38 ($COCH_3$), 55.20 ($ArOCH_3$), 56.58 (NCH_2), 75.53 (NCH), 80.33 ($COCH_3$), 111.42 (2 arom CH), 111.46 (2 arom CH), 138.82 (s, C=N), 142.47 (arom C–OCO), 143.61, 143.65 (arom $C-C(CH_3)_3$), 155.96 (arom $C-OCH_3$), 166.90 (CO_2Ar); MS (70 eV, EI): m/z (%): 488 (1.8) [M^+], 387 (72), 274 (56), 253 (100), 225 (20), 221 (11), 138 (48), 101 (23), 69 (50), 57 (78); IR ($CHCl_3$): $\tilde{\nu}$ = 2967, 1714, 1589, 1458, 1430, 1306, 1243, 1187, 1113 cm^{-1}; $C_{29}H_{48}N_2O_4$ (488.7): calcd C 71.27, H 9.90, N 5.73; found C 70.94, H 9.63, N 5.93.

(*S*)-(+)-1-[1-(2,6-Di-*tert*-butyl-4-methoxy-1-phenoxycarbonyl)-1-(2-phenyl)ethylideneamino]-2-(1-methoxy-1-ethylpropyl)pyrrolidine ((*S*)-6c): According to the general procedure, 2,6-di-*tert*-butyl-4-methoxyphenyl 2-oxo-3-phenylpropionate [(*S*)-**5c**, 9.60 g, 30 mmol] and SAEP (5.7 g, 31 mmol) were reacted in cyclohexane for 10 d. After work-up, purification of the crude product by flash column chromatography (silica gel, petroleum ether/ether 5:1) afforded the hydrazone (*S*)-**6c** as a pale yellow viscous oil (12.37 g, 75 %); $[\alpha]_D^{23} = +599.0$ (c = 1.02, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84, 0.85 (t, J = 7.4 Hz, 6H; $C(CH_2CH_3)_2$), 1.26, 1.35 (s, 18H; $2C(CH_3)_3$), 1.40–2.00 (m, 8H; CH_2CH_2, $2CH_2CH_3$), 3.09 (s, 3H), 3.05–3.10 (m, 1H; NCH_2CH_2), 3.60–3.70 (m, 1H; NCH_2CH_2), 3.78 (s, 3H; $ArOCH_3$), 3.94–4.00 (m, 1H; $NCHCH_2$), 4.0 (d, J = 16.2 Hz, 1H), 4.19 (d, J = 16.2 Hz, 1H), 6.85 (s, 2H; 2 arom CH (Ar)), 7.20–7.24 (m, 5H; 5 arom CH (Ph)); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 8.53, 8.75 ($2CH_2CH_3$), 23.94, 24.48 ($C(CH_2CH_3)_2$), 25.69 ($NCHCH_2$), 27.57 (NCH_2CH_2), 31.74, 32.01 ($C(CH_3)_3$), 35.29 (CH_2C=N), 36.21, 36.23 ($C(CH_3)_3$), 50.94 ($COCH_3$), 55.83 ($ArOCH_3$), 56.22 (NCH_2), 73.35 (NCH), 80.94 ($COCH_3$), 112.07 (2 arom CH), 126.78, 128.94, 129.13, 133.38 (C=N), 139.03, 143.21 (arom C–OCO), 144.20, 144.30 (arom $C-C(CH_3)_3$), 156.57 (arom $C-OCH_3$), 167.98 (C=O); IR (film): $\tilde{\nu}$ = 2967, 1711, 1560, 1454, 1251, 1217, 1171, 879, 667 cm^{-1}; MS (70 eV, EI): m/z (%) = 550 (2.5) [M^+], 449 (90), 315 (100), 287 (19), 138 (30), 57 (42); $C_{34}H_{50}N_2O_4$ (550.8): calcd C 74.14, H 9.15, N 5.09; found C 74.42, H 9.04, N 5.58.

Aldol reaction of the SAEP hydrazone (*S*)-6a (R = H); general procedure: A solution of LDA/LiBr was prepared by addition of *n*-butyllithium in *n*-hexane (1.6 M solution, 4.2 mL, 6.7 mmol) to a suspension of diisopropylamine hydrobromide (0.60 g, 3.3 mmol) in anhydrous THF (10 mL) at 0 °C under Ar. A solution of the hydrazone (*S*)-**6a** (3 mmol) in anhydrous THF (10 mL) was slowly added to the LDA/LiBr solution (3.3 mL, 3.3 mmol) at −78 °C. The reaction mixture was stirred at this temperature for 1–2 h. The resulting solution was cooled to −90 °C, and the aldehyde (3.1 mmol), dissolved in THF (2 mL), was added dropwise. The solution was kept at −90 °C for 1–2 h, warmed to −78 °C, kept for 1 h, and then hydrolyzed by addition of a saturated NH_4F solution (2 mL). The mixture was warmed to room temperature and diluted with ether (200 mL). The organic layer was washed with water, buffer solution (pH 7) and saturated NaCl solution (15 mL each), and dried with $MgSO_4$. The solvent was removed in vacuo and the aldol product purified by flash chromatography (silica gel, petroleum ether/ethyl acetate 4:1).

(*S,R*)-(+)-1-[3-Hydroxy-1-(2,6-di-*tert*-butyl-4-methoxy-1-phenoxycarbonyl)-1-heptylideneamino]-2-(1-ethyl-1-methoxypropyl)pyrrolidine ((*S,R*)-7a): Hydrazone (*S*)-**6a** (0.95 g, 2.0 mmol) was metalated with LDA/LiBr and reacted with *n*-pentanal (0.19 g, 2.2 mmol) as outlined above. Purification by flash chromatography (silica gel, petroleum ether/ethyl acetate 9:1) afforded the aldol product (*S,R*)-**7a** as a highly viscous yellow oil (0.94 g, 84 %); de = 93 % (^{1}H and ^{13}C NMR); $[\alpha]_D^{23} = +533.0$ (c = 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85, 0.87, 0.88 (3t, 3 × 3H; $C(CH_2CH_3)_2$),CH_3), 1.10–2.07 (complex, 14H; $C(CH_2CH_3)_2$), $(CH_2)_3CH_3$, $NCH_2CH_2CH_2$), 1.32, 1.36 (2s, 2 × 9H; $C(CH_3)_3$), 2.73 (dd, J = 14.9 Hz, J = 4.3 Hz, 1H; CHHC=N), 2.85 (m, 1H; OH), 2.86 (dd, J = 14.7 Hz, J = 8.2 Hz, 1H; CHHC=N), 3.26 (s, 3H; OCH_3), 3.37 (m, 1H; NCHH), 3.65 (m, 1H; NCHH), 3.78 (s, 3H; $ArOCH_3$), 3.97 (complex, 2H; CHOH, NCH), 6.86 (m, 2H; 2 arom CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.96, 8.19 ($2C(CH_2CH_3)_2$), 14.05 (CH_3), 22.67 ($CH_2CH_3)_2$), 23.72 ($NCHCH_2$), 24.11, 25.27 ($2C(CH_2CH_3)_2$), 26.88 (NCH_2CH_2), 28.06 ($CH_2CH_2CH_3$), 31.08, 31.40 ($2C(CH_3)_3$), 35.60, 35.70 ($2C(CH_3)_3$), 37.63 (CH_2CHOH), 38.11 (CH_2C=N), 50.30 (OCH_3), 55.15 ($ArOCH_3$), 56.76 (NCH_2), 69.20 (CHOH), 72.91 (NCH), 80.35 ($COCH_3$), 111.44, 111.52 (2 arom CH), 133.59 (CO_2Ar), 142.39 (arom C–OCO), 143.53, 143.67 (2 arom $C-C(CH_3)_3$), 156.06 (arom $C-OCH_3$), 168.19 (C=N); IR ($CHCl_3$): $\tilde{\nu}$ = 3444, 2960, 2874, 1714, 1589, 1566, 1458, 1430, 1420, 1364, 1303, 1252, 1218, 1173, 1115, 1070, 1021, 923, 879 cm^{-1}; $C_{33}H_{56}N_2O_5$ (560.8): calcd C 70.68, H 10.06, N 5.00; found C 70.49, H 10.22, N 5.00.

(*S,R*)-(+)-1-[3-Hydroxy-5-methyl-1-(2,6-di-*tert*-butyl-4-methoxy-1-phenoxycarbonyl)-1-hexylideneamino]-2-(1-ethyl-1-methoxypropyl)pyrrolidine ((*S,R*)-7b): Hydrazone (*S*)-**6a** (0.95 g, 2.0 mmol) was metalated with LDA/LiBr and reacted with 3-methylbutanal (0.19 g, 2.2 mmol) as outlined above. Purification by flash chromatography (silica gel, petroleum ether/ethyl acetate 4:1) afforded the aldol product (*S,R*)-**7b** as a highly viscous yellow oil (1.05 g, 94 %); de = 88 % (^{1}H NMR and ^{13}C NMR); $[\alpha]_D^{23} = +579.2$ (c = 1, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.88 (m, 12H; $CH(CH_3)_2$), $2CH_2CH_3$), 1.14–2.10 (complex, 7H; $CH(CH_3)_2$, $CH_2CH(CH_3)_2$, $NCH_2CH_2CH_2$), 1.32, 1.36 (s, 2 × 9H; $C(CH_3)_3$), 1.53, 1.76 (q, 2 × 2H; $2CH_2CH_3$), 2.60 (m, 1H; OH), 2.70 (dd, J = 14.8 Hz, J = 4 Hz, 1H; CHHC=N), 2.87 (dd, J = 14.8 Hz, J = 4 Hz, 1H; CHHC=N), 3.26 (s, 3H; OCH_3), 3.26 (m, 1H; NCHH), 3.63 (m, 1H; NCHH), 3.79 (s, 3H; $ArOCH_3$), 3.98 (m, 1H; NCH), 4.11 (m, 1H; CHOH), 6.87 (m, 2H; 2 arom H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.99, 8.21 ($2CH_2CH_3$), 21.86, 23.49 ($CH(CH_3)_2$), 23.79, 24.12 ($2CH_2CH_3$), 24.62 ($CH(CH_3)_2$), 25.29 ($NCHCH_2$), 26.87 (NCH_2CH_2), 31.10, 31.56 ($2C(CH_3)_3$), 35.60, 35.75 ($2C(CH_3)_3$), 38.55 (CH_2C=N), 47.16 (CH_2CHOH), 50.33 (OCH_3), 55.20 ($ArOCH_3$), 56.69 (NCH_2), 67.15 (CHOH), 72.98 (NCH), 80.39 ($COCH_3$), 111.48, 111.56 (2 arom CH), 133.59 (CO_2Ar), 142.37 (arom C–OCO), 143.53, 143.70 (2 arom $C-C(CH_3)_3$), 156.06 (arom $C-OCH_3$), 168.22 (C=N); IR (film): $\tilde{\nu}$ = 3450, 3004, 2966, 1703, 1589, 1561, 1467, 1450, 1430, 1366, 1304, 1217, 1185, 1174, 1142, 1068 cm^{-1}; $C_{33}H_{56}N_2O_5$ (560.8): calcd C 70.68, H 10.06, N 5.00; found C 70.65, H 9.81, N 5.09.

(*S,S*)-(+)-1-[3-Hydroxy-1-(2,6-di-*tert*-butyl-4-methoxy-1-phenoxycarbonyl)-3-(4-methylphenyl)-1-propylideneamino]-2-(1-ethyl-1-methoxypropyl)pyrrolidine ((*S,S*)-7c): Hydrazone (*S*)-**6a** (0.95 g, 2.0 mmol) was metalated with LDA/LiBr and reacted with 4-methylbenzaldehyde (0.26 g, 2.2 mmol) as outlined above. Purification by flash chromatography (silica gel, pentane/ethyl acetate 4:1) afforded the aldol product (*S,R*)-**7c** as a yellow highly viscous oil (1.09 g, 92 %); de > 98 % (^{1}H and ^{13}C NMR); $[\alpha]_D^{23} = +478.0$ (c = 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.83, 0.85 (2t, 2 × 3H; $C(CH_2CH_3)_2$), 1.35, 1.38 (2s, 2 × 9H; $C(CH_3)_3$), 1.46–2.04 (complex, 8H; $C(CH_2CH_3)_2$), $NCH_2CH_2CH_2$), 2.31 (s, 3H; $PhCH_3$), 2.91 (dd, J = 15.0 Hz and J = 3.7 Hz, 1H; CHHC=N), 3.10 (dd, J = 15.0 Hz, J = 5.2 Hz, 1H; CHHC=N), 2.85 (m, 1H; OH), 3.18 (m, 1H; NCHH), 3.19 (s, 3H; OCH_3), 3.56 (m, 2H; NCH, NCHH), 3.79 (s, 3H; $ArOCH_3$), 3.95 (m, 1H; CHOH), 5.10 (m, 1H; OH), 6.89 (m, 2H; 2 arom H (Ar)), 7.18 (m, 4H; 4 arom CH (*p*MePh)); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 7.99, 8.14 ($2C(CH_2CH_3)_2$), 21.08 ($C_6H_4CH_3$), 23.61 ($NCHCH_2$), 23.94, 25.20 ($2C(CH_2CH_3)_2$), 26.88 (NCH_2CH_2), 31.13, 31.54 ($2C(CH_3)_3$), 35.59, 35.76 ($2C(CH_3)_3$), 39.94 (CH_2C=N), 50.32 (OCH_3), 55.18 ($ArOCH_3$), 56.11 (NCH_2), 71.30 (CHOH), 72.85 (NCH), 80.45 ($COCH_3$), 111.48, 111.54 (2 arom CH (Ar)), 125.58 (2 arom *o*-CH (*p*MePh)), 129.07 (2 arom m-CH (*p*MePh)), 130.73 (CO_2Ar), 141.83 (arom C–OCO), 142.46 (arom C–CHOH), 143.58, 143.74 (2 arom $C-C(CH_3)_3$), 156.06 (arom $C-OCH_3$), 168.67 (C=N); IR ($CHCl_3$): $\tilde{\nu}$ = 3425, 2966, 2879, 1711, 1590, 1430, 1420, 1395, 1304, 1170, 1107, 1077, 939, 919, 878 cm^{-1}; $C_{36}H_{54}N_2O_5$ (594.8): calcd C 72.69, H 9.15, N 4.71; found C 72.69, H 9.26, N 4.78.

(*S,S*)-(+)-1-[3-Hydroxy-1-(2,6-di-*tert*-butyl-4-methoxy-1-phenoxycarbonyl)-3-phenyl-1-propylideneamino]-2-(1-ethyl-1-methoxypropyl)pyrrolidine

((*S,S*)-**7d**): Hydrazone (*S*)-**6a** (0.95 g, 2.0 mmol) was metalated with LDA/LiBr and reacted with benzaldehyde (0.23 g, 2.2 mmol) as outlined above. Purification by flash chromatography (silica gel, pentane/ethyl acetate 85:15) afforded the aldol product (*S,R*)-**7d** as a highly viscous yellow oil (1.10 g, 95 %); *de* > 98 % (^{1}H and ^{13}C NMR); $[\alpha]_D^{23} = +470.7$ (*c* = 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.83, 0.86$ (2t, 2 × 3H; $C(CH_2CH_3)_2$), 1.35, 1.38 (2s, 2 × 9H; $C(CH_3)_3$), 1.40–2.08 (complex, 8H; $C(CH_2CH_3)_2$), $NCH_2CH_2CH_2$), 2.91 (dd, *J* = 15.0 Hz, *J* = 3.7 Hz, 1H; C*H*HC=N), 3.10 (dd, *J* = 15.0 Hz, *J* = 5.2 Hz, 1H; CH*H*C=N), 3.18 (m, 1H; NC*H*H), 3.19 (s, 3H; OCH_3), 3.56 (m, 2H; NCH, NCH*H*), 3.79 (s, 3H; $ArOCH_3$), 3.95 (m, 1H; C*H*OH), 5.10 (m, 1H; OH), 6.89 (m, 2H; 2arom CH (Ar)), 7.30 (m, 5H; 5arom CH (Ph)); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 8.00$, 8.18 ($2C(CH_2CH_3)_2$), 23.73 ($NCHCH_2$), 23.99, 25.22 ($2C(CH_2CH_3)_2$), 26.87 (NCH_2CH_2), 31.15, 31.55 ($2C(CH_3)_3$), 35.68, 35.78 ($2C(CH_3)_3$), 36.97 (CH_2C=N), 50.34 (OCH_3), 55.23 ($ArOCH_3$), 56.17 (NCH_2), 71.51 (CHOH), 72.91 (NCH), 80.45 ($COCH_3$), 111.52, 111.58 (2arom *C*H (Ar)), 125.61 (2arom *o*-CH (Ph)), 127.41 (arom *p*-CH (Ph)), 128.43 (arom *m*-CH (Ph)), 130.70 (CO_2Ar), 142.43 (arom *C*–OCO), 143.58, 143.75 (2arom *C*-$C(CH_3)_3$), 144.72 (arom *C*-CHOH), 156.09 (arom *C*–OCH_3), 168.77 (C=N); IR ($CHCl_3$): $\tilde{\nu} = 3441$, 2969, 2881, 1700, 1589, 1455, 1430, 1420, 1302, 1184, 1172, 1107, 1088, 1070, 702 cm^{-1}; $C_{35}H_{52}N_2O_5$ (580.8): calcd C 72.38, H 9.02, N 4.82; found C 72.38, H 9.05, N 4.82.

(*S,S,R*)-(+)-[4,5]-*O*-Cyclohexylidene-3,4,5-trihydroxy-1-(2,6-di-*tert*-butyl-4-methoxy-1-phenoxycarbonyl)-1-pentylideneamino]-2-(1-ethyl-1-methoxypropyl)pyrrolidine ((***S,S,R*)-7e**): Hydrazone (*S*)-**6a** (1.80 g, 3.92 mmol) was metalated and reacted with 2,3-*O*-cyclohexylidene-2,3-dihydroxy aldehyde (0.77 g, 4.50 mmol) as outlined above. Purification by flash chromatography afforded the aldol product (*S,S,R*)-**7e** (1.15 g, 47 %) as a a yellow foam along with the furanone (*S,S,R*)-**8e** (0.69 g, 45 %).

(***S,S,R*)-7e**: *de* > 98 % (^{1}H NMR and ^{13}C NMR); $[\alpha]_D^{23} = +503.0$ (*c* = 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.85$, 0.86 (t, *J* = 7.3 Hz, 6H; $C(CH_2CH_3)_2$), 1.32, 1.36 (s, 18H; $2C(CH_3)_3$), 1.50–2.10 (complex, 18H; NCH_2CH_2, $2C(CH_2CH_3)_2$), 5 CH_2 (*c*-hexyl)), 2.75 (dd, *J* = 15.3 Hz, *J* = 9.5 Hz, 1H; C*H*HC=N), 3.12 (dd, *J* = 15.3 Hz, *J* = 2.44 Hz, 1H; CH*H*C=N), 3.26 (s, 3H; OCH_3), 3.39–3.41 (m, 1H; NCH_2CH_2), 3.50 (s, 1H; OH), 3.80 (s, 3H; $ArOCH_3$), 3.80–3.83 (m, 1H; NCH_2CH_2), 3.99–4.01 (m, 3H; NCH, OCH_2CHO), 4.09 (dd, *J* = 8.3 Hz, *J* = 6.1 Hz, 1H; OC*H*CH_2C=N), 6.86, 6.88 (d, *J* = 3 Hz, 2H; 2arom CH); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta =$ 7.99, 8.25 ($2C(CH_2CH_3)_2$), 23.78 (CH_2, *c*-hexyl), 23.89, 24.02 ($2CH_2CH_3$), 25.17 ($NCHCH_2$), 25.19 (CH_2, *c*-hexyl), 26.82 (NCH_2CH_2), 31.15, 31.48 ($2C(CH_3)_3$), 34.24 (CH_2C=N), 34.62 (t), 35.61, 35.76 (s, $C(CH_3)_3$), 36.34 (CH_2, *c*-hexyl), 50.40 ($COCH_3$), 55.23 ($ArOCH_3$), 56.17 (NCH_2), 66.52 (OCH_2CHO), 71.07 (CHOH), 72.93 (NCH), 78.37 (OCH), 80.49 ($COCH_3$), 109.79 (OCO), 111.55, 111.63 (2arom *CH*), 131.62 (CO_2Ar), 142.32 (arom *C*–OCO), 143.60, 143.73 (arom *C*–$C(CH_3)_3$), 156.19 (arom *C*–OCH_3), 169.65 (C=N); MS (70 eV, EI): *m/z* (%) = 543 (19), 377 (16), 307 (22), 141 (63), 127 (100), 99 (17), 85 (14), 81 (31); IR (film): $\tilde{\nu} = 3500$, 2939, 1707, 1509, 1479, 1448, 1303, 1183, 1171, 1086, 679 cm^{-1}; $C_{37}H_{60}N_2O_7$ (644.9): calcd C 68.90, H 9.38, N 4.35; found C 68.41, H 9.40, N 4.16.

Lactonization of the SAEP hydrazones 7a–e to the hydrazonolactones 8a–e; general procedure: For the lactonization, the hydrazones **7a–e** (2 mmol) were dissolved in anhydrous THF (20 mL) under Ar. The solution was cooled to −78 °C and a solution of *tert*-butyllithium (1.6 M) in *n*-hexane (1.25 mL, 2.0 mmol) or *t*BuOK (0.224 g, 2.0 mmol) was added. The reaction mixture was warmed to −10 °C and stirred at this temperature until tlc indicated complete reaction. The solution was hydrolyzed by the addition of saturated NH_4Cl solution (10 mL) and then diluted with ether (100 mL). The organic layer was washed with water, saturated NaCl solution, and dried with $MgSO_4$. After removal of the solvent in vacuo, the hydrazonolactones **8a–e** were isolated by flash chromatography (silica gel, petroleum ether/ether 1:1).

(*S,R*)-(+)-5-Butyl-*N*-[2-(1-ethyl-1-methoxypropyl)pyrrolidine]-3-iminodihydro-2-furanone ((***S,R*)-8a**): The aldol product (*S,R*)-**7a** (1.24 g, 2.20 mmol) was cyclized with *t*BuLi as the base as outlined above. After column chromatography, the furanone (*S,R*)-**8a** was isolated as a white solid (0.60 g, 84 %). M.p. 72–73 °C. Some starting aldol product (*S,R*)-**7a** was recovered (0.14 g, 10 %). $[\alpha]_D^{23} = +1017$ (*c* = 1, $CHCl_3$); *de* ≥ 98 % (^{1}H and ^{13}C NMR); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.86$, 0.89 (t, *J* = 7.6 Hz, 6H; $C(CH_2CH_3)_2$), 0.92 (t, *J* = 7.0 Hz, 3H; $CH_2CH_2CH_3$), 1.35–1.53 (m, 4H; $CH_2CH_2CH_3$), 1.60–1.75 (m, 6H; $2CH_2CH_3$, $CH_2CH_2CH_2$), 1.75–2.10 (m, 4H; CH_2CH_2), 2.77 (dd, *J* = 17.1 Hz, *J* = 6.4 Hz, 1H; $CHCH_2C$=N), 3.02 (dd, *J* = 17.1 Hz, *J* = 7.63 Hz, 1H; $CHCH_2C$=N), 3.17–3.20 (m, 1H; NCH_2CH_2), 3.27 (s, 3H; OCH_3), 3.70–3.74 (m, 1H; NCH_2CH_2), 4.0–4.3 (m, 1H; $NCHCH_2$), 4.48–4.50 (m, 1H; $OCHCH_2$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 8.00$, 8.26 ($2CH_2CH_3$), 13.95 ($H_3CCH_2CH_2$), 22.44 ($H_3CCH_2CH_2$), 23.91, 24.02 ($2CCH_2CH_3$), 24.75 ($NCHCH_2$), 26.50 (NCH_2CH_2), 26.86 ($H_3CCH_2CH_2$), 34.29 (t, CH_2C=N), 36.38 ($CH_2CH_2CH_2$), 50.50 ($COCH_3$), 53.75 (NCH_2), 71.81 (NCH), 76.17 (OCH), 80.47 ($COCH_3$), 127.48 (C=N), 168.85 (C=O); MS (70 eV, EI): *m/z* (%) = 324 (0.91) [M^+], 223 (69), 179 (11), 111 (14), 101 (48), 70 (100), 45 (17), 41 (24); IR (film): $\tilde{\nu} = 2890$, 1752, 1588, 1346, 1247, 1203, 1088, 1005 cm^{-1}; $C_{18}H_{32}N_2O_3$ (324): calcd C 66.63, H 9.94, N 8.64; found C 66.67, H 10.12, N 8.69.

(*S,R*)-(+)-*N*-[2-(1-Ethyl-1-methoxypropyl)pyrrolidine]-3-imino-5-(2-methylpropyl)dihydro-2-furanone ((***S,R*)-8b**): The aldol product (*S,R*)-**7b** (1.33 g, 2.37 mmol) was cyclized with *t*BuOK as base, as outlined above. After column chromatography, the furanone (*S,R*)-**8b** was isolated as a yellow foam (0.61 g, 80 %). $[\alpha]_D^{23} = +902$ (*c* = 0.99, $CHCl_3$); *de* ≥ 98 % (^{1}H and ^{13}C NMR); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.87$, 0.89 (t, *J* = 7.4 Hz, 6H; $C(CH_2CH_3)_2$), 0.96 (d, *J* = 6.9 Hz, 3H), 0.98 (d, *J* = 6.9 Hz; 3H), 1.35–1.48 (m, 3H), 1.52–1.72 (m, 6H), 1.80–1.90 (m, 3H; CH_2CH_2, $CH(CH_3)_2$), 1.9–2.2 (m, 2H; CH_2CH_2), 2.76 (dd, *J* = 17 Hz, *J* = 6.64 Hz, 1H; C*H*HC=N), 3.06 (dd, *J* = 17 Hz, *J* = 7.4 Hz, 1H; CH*H*C=N), 3.20–3.25 (m, 1H; NC*H*HCH_2), 3.27 (s, 3H; OCH_3), 3.71–3.74 (m, 1H; $NCHHCH_2$), 3.98–4.00 (m, 1H; $NCHCH_2$), 4.48–4.50 (m, 1H; $OCHCH_2$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 7.98$, 8.23 ($2CH_2CH_3$), 22.13, 22.98 ($CH(CH_3)_2$), 23.86, 23.99 ($2CH_2CH_3$), 24.57 ($CH(CH_3)_2$), 24.70 ($NCHCH_2$), 26.45 (NCH_2CH_2), 34.77 (CH_2C=N), 45.92 ($(H_3C)_2CHCH_2$), 50.41 ($COCH_3$), 53.69 (NCH_2), 71.70 (NCH), 74.71 (OCH), 80.36 ($COCH_3$), 127.36 (C=N), 168.76 (C=O); MS (70 eV, EI): m/z (%) = 324 (0.91) [M^+], 295 (11), 223 (100), 168 (10); IR (film): $\tilde{\nu} = 2961$, 1760, 1582, 1213, 1185, 1150, 1079 cm^{-1}; $C_{18}H_{32}N_2O_3$ (324): calcd C 66.63, H 9.94, N 8.64; found C 66.38, H 10.22, N 9.04.

(*S,S*)-(+)-*N*-[2-(1-Ethyl-1-methoxypropyl)pyrrolidine]-3-imino-5-(4-methylphenyl)-dihydro-2-furanone ((***S,S*)-8c**): The aldol product (*S,R*)-**7c** (1.19 g, 2.00 mmol) was cyclized with *t*BuLi as the base, as outlined above. After column chromatography, the furanone (*S,R*)-**8c** was isolated as a yellow foam (0.52 g, 72 %). Some starting aldol product (*S,R*)-**7c** was recovered (0.09 g, 7.5 %). $[\alpha]_D^{23} = +845$ (*c* = 1, $CHCl_3$); *de* ≥ 98 % (^{1}H and ^{13}C NMR); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.89$, 0.92 (t, *J* = 7.4 Hz, 6H; $C(CH_2CH_3)_2$), 1.40–1.80 (m, 4H; $2CH_2CH_3$), 1.8–2.1 (m, 4H; CH_2CH_2), 2.36 (s, 3H; $PhCH_3$), 3.07 (dd, *J* = 17 Hz, *J* = 6.9 Hz, 1H; $CHCH_2C$=N), 3.18–3.30 (m, 1H; NCH_2CH_2), 3.27 (s, 3H; OCH_3), 3.37 (dd, *J* = 17 Hz, *J* = 7.97 Hz, 1H; $CHCH_2C$=N), 3.67–3.69 (m, 1H; NCH_2CH_2), 4.00–4.10 (m, 1H; $NCHCH_2$), 5.64 (dd, *J* = 7.97 Hz, *J* = 6.9 Hz, 1H; $OCHCH_2$), 7.19, 7.23 (d, *J* = 8.3 Hz, 4H; C_6H_4); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 8.00$, 8.29 ($2CH_2CH_3$), 21.16 ($ArCH_3$), 23.95, 23.98 ($2CH_2CH_3$), 24.65 ($NCHCH_2$), 26.48 (NCH_2CH_2), 37.04 (CH_2C=N), 50.49 ($COCH_3$), 53.59 (NCH_2), 71.72 (NCH), 77.68 (OCH), 80.47 ($COCH_3$), 125.33 (2arom *m*-CH (*p*MePh)), 125.96 (C=N), 129.48 (2arom *o*-CH (*p*MePh)), 137.38 (arom *p*-C (*p*MePh)), 138.35 (arom C (*p*MePh)), 168.64 (C=O); MS (70 eV, EI): *m/z* (%) = 358 (0.51) [M^+], 257 (72), 213 (33), 144 (17), 117 (13), 105 (36), 101 (52), 70 (100), 45 (19), 41 (15); IR ($CHCl_3$): $\tilde{\nu} = 2942$, 1757, 1577, 1459, 1322, 1214, 1179, 1084, 1022, 821, 755 cm^{-1}; $C_{21}H_{30}N_2O_3$ (358.5): calcd C 70.36, H 8.44, N 7.82; found C 70.48, H 8.50, N 7.98.

(*S,S*)-(+)-*N*-[2-(1-Ethyl-1-methoxypropyl)pyrrolidine]-3-imino-5-phenyldihydro-2-furanone ((***S,S*)-8d**): The aldol product (*S,R*)-**7d** (1.70 g, 2.93 mmol) was cyclized with *t*BuLi as the base, as outlined above. After column chromatography, the furanone (*S,S*)-**8d** was isolated as a yellow foam (0.72 g, 72 %). Some starting aldol product (*S,R*)-**7d** was recovered (0.17 g, 10 %). $[\alpha]_D^{23} = +857$ (*c* = 0.99, $CHCl_3$); *de* ≥ 98 % (^{1}H and ^{13}C NMR); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.88$, 0.92 (t, *J* = 7.4 Hz, 6H; $C(CH_2CH_3)_2$), 1.45–1.80 (m, 4H; $2CH_2CH_3$), 1.8–2.0 (m, 4H; CH_2CH_2), 3.08 (dd, *J* = 17 Hz, *J* = 6.9 Hz, 1H; $CHCH_2C$=N), 3.12–3.20 (m, 1H; NC*H*HCH_2), 3.28 (s, 3H; OCH_3), 3.41 (dd, *J* = 17 Hz, *J* = 8.24 Hz, 1H; $CHCH_2C$=N), 3.67–3.70 (m, 1H; $NCHHCH_2$), 3.95–4.05 (m, 1H; $NCHCH_2$), 5.47 (dd, *J* = 8.24 Hz, *J* = 6.9 Hz, 1H; $OCHCH_2$), 7.36 (m, 5H; C_6H_5); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 8.00$, 8.29 ($2CH_2CH_3$), 23.91, 23.95 ($2CH_2CH_3$), 24.59 ($NCHCH_2$), 26.46 (NCH_2CH_2), 36.91 (CH_2C=N), 50.45 ($COCH_3$), 53.51 (NCH_2), 71.64 (NCH), 76.62 (OCH), 80.40 ($COCH_3$), 125.30 (2arom *m*-CH), 125.49 (C=O), 128.44 (arom *p*-CH), 128.82 (2arom *o*-CH), 140.40 (arom C), 168.55 (C=N); MS (70 eV, EI): *m/z*

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(%) = 328 (0.88) [M^+], 199 (37), 125 (6.4), 111 (10), 101 (19), 73 (20), 61 (23), 57 (14), 43 (100); IR (film): $\tilde{\nu}$ = 2883, 1754, 1575, 1457, 1216, 1029, 757 cm^{-1}; $C_{20}H_{28}N_2O_3$ (344.5): calcd C 69.74, H 8.19, N 8.13; found: C 69.98, H 8.20, N 8.04.

(*S*,*S*,*R*)-(+)-5-*O*-Cyclohexylidenedioxyethyl-*N*-[2-(1-ethyl-1-methoxypropyl)-pyrrolidine]-3-iminodihydro-2-furanone (**(*S*,*S*,*R*)-8e**): The aldol product (*S*,*S*,*R*)-**7e** (720 mg, 1.11 mmol) was cyclized with *t*BuLi as the base, as outlined above. After column chromatography, the furanone (*S*,*S*,*R*)-**8e** was isolated as a yellow foam (0.38 g, 92%); *de* ≥ 98% (^{1}H NMR and ^{13}C NMR); $[\alpha]_D^{23} = +575$ (*c* = 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.87, 0.90 (t, *J* = 7.3 Hz, 6H; C(CH_2CH_3)$_2$), 1.4–1.7 (m, 14H; 2CH_2CH_3, 5CH_2 (cyclohexyl), 1.8–2.1 (m, 4H; CH_2CH_2), 3.02 (dd, *J* = 17.4 Hz, *J* = 7.9 Hz, 1H; CHCH_2C=N), 3.14 (dd, *J* = 17.4 Hz, *J* = 5.2 Hz, 1H; CHCH_2C=N), 3.25–3.27 (m, 1H; NCH_2CH$_2$), 3.26 (s, 3H; OCH_3), 3.76–3.82 (m, 1H; NCH_2CH$_2$), 3.96–4.02 (m, 2H; NC*H*CH$_2$, OCH_2CHO), 4.13–4.16 (m, 2H; OCH_2C*H*O), 4.39 (m, 1H; OC*H*CH$_2$C=N); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 7.98, 8.29 (2CH_2CH_3), 23.71 (CH_2, *c*-hexyl), 23.94 (CH_2, *c*-hexyl), 23.98, 24.01 (2CH_2CH_3), 24.65 (NCHCH_2), 25.08 (CH_2, *c*-hexyl), 26.48 (NCH_2CH_2), 30.56 (CH_2, *c*-hexyl), 34.45 (CH_2C=N), 36.55 (CH_2, *c*-hexyl), 50.49 (COCH_3), 53.52 (NCH_2), 66.51 (OCH_2CHO), 71.72 (N*CH*), 75.58(OCH$_2$*C*HO), 77.00 (O*CH*), 80.48 (*C*OCH$_3$), 110.64 (O*CO*), 124.98 (C=N), 168.26 (C=O); MS (70 eV, EI): *m*/*z* (%) = 409 (1.17) [M^+], 377 (61), 307 (70), 236 (27), 168 (11), 138 (21), 127 (32), 91 (26), 81 (26), 55 (49); IR ($CHCl_3$): $\tilde{\nu}$ = 2939, 1761, 1578, 1214, 1181, 1163, 1097, 925, 756 cm^{-1}; $C_{22}H_{36}N_2O_5$ (408.5): calcd C 64.68, H 8.89, N 6.86; found: C 64.51, H 8.73 N 6.70.

Aldol reaction and lactonization of the SAEP hydrazone (*S*)-6b (R = Me) and (*S*)-6c (R = Ph); general procedure: The metalation and aldol addition of the hydrazones (*S*)-**6b** and (*S*)-**6c** were performed under the same conditions as described above for the hydrazone(*S*)-**6a**, except that 30–50% DMPU were added as a cosolvent. After the aldol addition, the aldol products were not isolated, but cyclized in situ by warming the reaction mixture after 0.5 h from −78 °C to −10 °C. The solution was stirred at −10 °C until the reaction was complete (3–4 h), as indicated by tlc, and then hydrolyzed by addition of saturated NH_4Cl solution. The hydrazonolactones **8f–h** were purified by flash chromatography.

(*S*,*S*,*S*)-*N*-[2-(1-Ethyl-1-methoxypropyl)pyrrolidine]-3-imino-4-methyl-5-(4-methylphenyl)dihydro-2-furanone (**(*S*,*S*,*S*)-8f**): As outlined above, the hydrazone (*S*)-**6b** (0.30 g, 0.61 mmol) was metalated with LDA/LiBr (0.79 mmol) in anhydrous THF (5 mL)/DMPU (2.5 mL) and then reacted with 4-methylbenzaldehyde (0.10 g, 0.8 mmol). Purification of the crude product by flash chromatography (silica gel, petroleum ether/diethyl ether 1:1) afforded the furanone (*S*,*S*,*S*)-**8f** as mixture of the (*S*,*S*,*S*)-isomer (*syn*) and the (*S*,*R*,*S*)-isomer (*anti*) (0.12 g, 54%; ratio (*S*,*S*,*S*)/(*S*,*R*,*S*) 21:1).

(*S*,*S*,*S*)-8f: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.88, 0.91 (t, *J* = 7.6 Hz, 6H; C(CH_2CH_3)$_2$), 1.33 (d, *J* = 7.02 Hz, 3H; H_3CCHC=N), 1.40–1.70 (m, 4H; 2CH_2CH_3), 1.85–2.08 (m, 4H; CH_2CH_2), 2.34 (s, 3H; C_6H_4-CH_3), 2.90–2.98 (m, 1H; NC*H*HCH$_2$), 3.17 (qd, *J* = 7.02 Hz, *J* = 2.45 Hz, 1H; H_3CC*H*C=N), 3.24 (s, 3H; OCH_3), 3.49–3.53 (m, 1H; NCH*H*CH$_2$), 4.00–4.07 (m, 1H; NC*H*CH$_2$), 5.10 (d, *J* = 2.45 Hz, 1H; C*H*-C_6H_4), 7.18, 7.19 (d, *J* = 8.5 Hz, 4H; *o,m* arom CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.97, 8.27 (2CH_2CH_3), 18.30 (H_3*C*CHC=N), 21.49 (H_3*C*-C_6H_4), 23.69, 23.95, (C(*C*H$_2$CH$_3$)$_2$), 24.62 (NCH*C*H$_2$), 26.63 (NCH$_2$*C*H$_2$), 42.03 (H_3*C*CHC=N), 50.46 (CO*C*H$_3$), 53.78 (N*C*H$_2$), 72.39 (N*C*H), 80.63 (*C*OCH$_3$), 83.96 (O*C*H), 125.10 (2arom *o*-CH), 130.0 (2arom *m*-CH), 130.19 (C=O), 137.74 (arom C–CH_3), 138.40 (arom C), 168.42 (C=N); MS (70 eV, EI): *m*/*z* (%) = 372 (1.6) [M^+], 271 (100), 253 (18), 227 (15), 158 (11), 101 (31), 91 (8.9), 70 (69), 58 (6); IR ($CHCl_3$): $\tilde{\nu}$ = 2970, 1757, 1576, 1452, 1244, 1212, 1184, 1077, 819, 757 cm^{-1}; $C_{22}H_{32}N_2O_3$ (372.1): C 70.93, H 8.66, N 7.52; found: C 70.96, H 8.82, N 7.21.

(*S*,*R*,*S*)- and (*S*,*S*,*S*)-*N*-[2-(1-Ethyl-1-methoxypropyl)pyrrolidine]-3-imino-4-phenyl-5-(4-methylphenyl)-dihydro-2-furanone (**(*S*,*S*,*S*)-8g**): As outlined above, the hydrazone (*S*)-**6c** (0.32 g, 0.65 mmol) was metalated with LDA/LiBr (0.77 mmol) in anhydrous THF (4 mL)/DMPU (1.5 mL) and reacted with 4-methylbenzaldehyde (0.10 g, 0.8 mmol). Purification of the crude product by flash chromatography (silica gel, petroleum ether/diethyl ether 1:1) afforded the furanone **8g** as a mixture of the (*S*,*S*,*S*)-isomer (*syn*) and the (*S*,*R*,*S*)-isomer (*anti*) (0.25 g, 88%; ratio (*S*,*S*,*S*)/(*S*,*R*,*S*) 4:3).

(*S*,*S*,*S*)-8g: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.75, 0.82 (t, *J* = 7.4 Hz, 6H; C(CH_2CH_3)$_2$), 1.40–1.90 (m, 8H; CH_2CH_2, 2CH_2CH_3), 2.37 (s, 3H; ArCH_3), 2.70 (s, 3H; OCH_3), 3.00–3.18 (m, 2H; NCH_2CH$_2$), 3.95–4.00 (m, 1H; NC*H*CH$_2$), 4.24 (d, *J* = 3.97 Hz, 1H; PhCH), 5.25 (d, *J* = 3.97 Hz, 1H; *p*MePhCH), 7.19 (s, 5H; 5arom CH (Ph)), 7.32, 7.35 (d, *J* = 7.6 Hz, 4H; 4arom *o,m*-CH (*p*MePh)); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 7.92, 7.94 (2CH_2CH_3), 21.19 (H_3*C*Ph), 22.85 (NCH*C*H$_2$), 23.68, 24.42 (2*C*H$_2$CH$_3$), 26.96 (NCH$_2$*C*H$_2$), 50.19 (CO*C*H$_3$), 53.84 (N*C*H$_2$), 54.04 (Ph*C*H), 72.40 (N*C*H), 80.42 (*C*OCH$_3$), 85.16 (d, O*C*H), 125.19 (2arom m-CH (*p*MePh)), 125.76 (C=O), 127.35 (2arom *o*-CH (*p*MePh)), 127.94 (arom *p*-CH (Ph)), 129.51 (2arom *m*-CH (Ph)), 129.66 (2arom *o*-CH (Ph)), 137.45 (arom *C*-CH (Ph)), 138.45 (arom *C*-CH_3), 140.41 (arom *C*-CH (*p*MePh)), 168.83 (C=N); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 8.06, 8.39 (2CH_2CH_3), 21.08 (H_3*C*Ph), 23.70 (NCH*C*H$_2$), 24.16, 24.40 (2*C*H$_2$CH$_3$), 26.51 (NCH$_2$*C*H$_2$), 50.54 (CO*C*H$_3$), 51.28 (Ph*C*H), 52.80 (N*C*H$_2$), 71.15 (N*C*H), 80.90 (*C*OCH$_3$), 82.23 (O*C*H), 125.56 (C=O), 126.18 (2arom *m*-CH (Ph)), 127.00 (2arom *p*-CH (Ph)), 128.34 (2arom *m*-CH (*p*MePh)), 128.48 (2arom *o*-CH (Ph)), 128.63 (2arom *o*-CH (*p*MePh)), 132.65 (arom *C* (Ph)), 138.48 (arom *C*-CH_3), 139.38 (arom *C*–CH (*p*MePh)), 170.15 (C=N); MS (70 eV, EI): *m*/*z* (%) = 434 (0.86) [M^+], 333 (100), 218 (13), 194 (15), 178 (11), 116 (18), 70 (69); IR (film): $\tilde{\nu}$ = 2966, 1741, 1655, 1558 (br), 1518, 1493, 1453, 1319, 1214, 1175, 1078, 1009, 826, 812, 725, 702 cm^{-1}; $C_{27}H_{34}N_2O_3$ (434.6): C 74.62, H 7.89, N 6.45; found: C 74.31, H 7.93, N 6.48.

(*S*,*R*,*S*)-8g: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.90, 0.96 (t, *J* = 7.3 Hz, 6H; C(CH_2CH_3)$_2$), 1.40–1.90 (m, 8H; CH_2CH_2, 2CH_2CH_3), 2.19 (s, 3H; ArCH_3), 3.10–3.16 (m, 1H; NCH_2CH$_2$), 3.29 (s, 3H; OCH_3), 3.50–3.54 (m, 1H; NCH_2CH$_2$), 3.95–4.00 (m, 1H; NC*H*CH$_2$), 4.51 (d, *J* = 6.4 Hz, 1H; PhCH), 5.68 (d, *J* = 6.4 Hz, 1H; *p*MePhCH), 6.78–6.80 (m, 2H; 2arom *o*-CH (Ph)), 6.81, 6.87 (d, *J* = 7.9 Hz, 4arom *m,o*-CH (*p*MePh), 7.02 (m, 3H; 3arom *m,p*-CH (Ph)).

(*S*,*R*,*R*)- and (*S*,*S*,*R*)-*N*-[2-(1-Ethyl-1-methoxypropyl)pyrrolidine]-3-imino-5-(2-methylethyl)-4-phenyldihydro-2-furanone (**(*S*,*R*,*R*)-/(*S*,*S*,*R*)-8h**): As outlined above, the hydrazone (*S*)-**6c** (1.10 g, 2.0 mmol) was metalated with LDA/LiBr (2.2 mmol) in anhydrous THF (12 mL)/DMPU (4.5 mL) and then reacted with 3-methylbutyric aldehyde (0.22 g, 2.5 mmol). Purification of the crude product by flash chromatography (silica gel, petroleum ether/diethyl ether 4:1) afforded the furanone **8h** as mixture of the *anti* (*S*,*R*,*R*)-, *syn* (*S*,*S*,*R*)- and *anti* (*S*,*S*,*S*)-isomer [(*S*,*R*,*R*)-**8h**: 400 mg, 50%; (*S*,*S*,*R*)-**8h**: 100 mg, 13%; (*S*,*S*,*S*)-**8h**: 40 mg, 5%; ratio (*S*,*R*,*R*)/(*S*,*R*,*S*)/(*S*,*S*,*S*) 10:2.6:1].

(*S*,*R*,*R*)-8h: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.72, 0.80 (t, *J* = 7.7 Hz, 6H; C(CH_2CH_3)$_2$), 0.90, 092 (d, *J* = 7.5 Hz, 6H; C(CH_3)$_2$), 1.30–1.98 (m, 11H; CH_2CH_2, 2CH_2CH_3, CH_2CH(CH_3)$_2$), 2.67 (s, 3H; OCH_3), 3.05–3.25 (m, 2H; NCH_2CH$_2$), 3.90–4.00 (m, 1H; NC*H*CH$_2$), 3.97 (d, *J* = 3.84 Hz, 1H; PhCH), 4.30–4.40 (m, 1H; OC*H*CH$_2$), 7.17 (d, *J* = 7.3 Hz, 2H; 2arom *o*-*CH*), 7.22–7.35 (m, 3H; 3arom *m*/*p*-CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 8.41, 8.48 (2CH_2CH_3), 22.43, 23.62 ((H_3C_2CH), 23.26, 24.24 (2*C*H$_2$CH$_3$), 25.08 (NCH*C*H$_2$), 25.08 ((H$_3$C)$_2$*C*H), 27.52 (NCH$_2$*C*H$_2$), 46.21 ((H$_3$C)$_2$CH*C*H$_2$), 50.71 (H*C*Ph), 51.94 (CO*C*H$_3$), 54.49 (N*C*H$_2$), 73.01 (N*C*H), 80.90 (O*C*H), 83.67 (*C*OCH$_3$), 127.66 (C=O), 127.76 (2arom *m*-CH), 128.30 (arom *p*-CH), 129.85 (2arom *o*-CH), 140.88 (arom *C*–CH), 169.21 (C=N).

(*S*,*S*,*R*)-8h: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.80, 1.00 (m, 12H; C(CH_2CH_3)$_2$), 1.48–1.98 (m, 11H; CH_2CH_2, 2CH_2CH_3, CH_2CH(CH_3)$_2$), 2.89–2.92 (m, 1H; NCH_2CH$_2$), 3.27 (s, 3H; OCH_3), 3.50–3.60 (m, 1H; NCH_2CH$_2$), 3.90–4.00 (m, 1H, NC*H*CH$_2$; 4.26), 4.24 (d, *J* = 6.32 Hz, 1H; PhCH), 4.66–4.70 (m, 1H; OC*H*CH$_2$), 7.10 (d, *J* = 7.7 Hz, 2H; 2arom *o*-CH), 7.20–7.35 (m, 3H; 3arom *m*/*p*-CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 8.51, 8.87 (2CH_2CH_3), 22.40, 23.79 ((H_3C)$_2$CH), 24.13, 24.56 (2*C*H$_2$CH$_3$), 24.94 (NCH*C*H$_2$), 25.29 ((H$_3$C)$_2$*C*H), 27.01 (NCH$_2$*C*H$_2$), 41.26 ((H$_3$C)$_2$CH*C*H$_2$), 49.64 (H*C*Ph), 50.94 (CO*C*H$_3$), 53.76 (N*C*H$_2$), 71.69 (N*C*H), 79.52 (O*C*H), 81.22 (*C*OCH$_3$), 127.37 (C=O), 127.91 (arom *p*-*CH*), 128.80 (2arom *m*-*CH*), 129.34 (2arom *o*-*CH*), 140.52 (arom *C*–CH), 170.60 (C=N); MS (70 eV, EI): *m*/*z* (%) = 400 (0.75) [M^+], 299 (77), 146 (24), 117 (18), 70 (100), 44 (21), 41 (17); IR (film): $\tilde{\nu}$ = 2960, 1751, 1567, 1465, 1455, 1217, 1181, 1088, 756 cm^{-1}; $C_{24}H_{36}N_2O_3$ (400.6): calcd C 71.96, H 9.06, N 7.00; found C 71.90, H 9.25, N 6.81.

Ozonolysis of the hydrazones 8 and introduction of the *t*BuMeSi protecting group; general procedure: For the cleavage of the chiral auxiliary, the hydrazones **8** (1 mmol) were dissolved in CH_2Cl_2 (50 mL) and cooled to −78 °C. Ozone was passed through the solution at this temperature until the reaction was complete (tlc). Excess ozone was removed by purging with a stream of Ar. For the introduction of the silyl protecting group, *t*-butyldimethylsilyl chloride (0.30 g, 2.0 mmol) and imidazole (0.15 g,

3.0 mmol) were added and the solution was warmed to room temperature. After complete reaction, the solution was concentrated and the products **9** purified by flash chromatography (silica gel, petroleum ether/ether 4:1).

(*R*)-(−)-5-Butyl-3-*t*-butyldimethysilyloxy-2(5*H*)-furanone ((*R*)-9a): The hydrazone (*S,R*)-**8a** (0.320 g, 1.02 mmol) was treated with ozone and *tert*-butyldimethylsilyl chloride, as described above. After column chromatography, the furanone (*R*)-**9a** was obtained as a colorless crystalline solid (0.20 g, 72%). M.p. 44.5–45.0 °C; $[\alpha]_D^{23} = -8$ ($c = 0.85$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.25$ (s, 6H; Si(CH_3)$_2$), 0.91 (t, $J = 6.9$ Hz, 3H; $CH_2CH_2CH_3$), 0.97 (s, 9H; SiC(CH_3)$_3$), 1.3–1.45 (m, 4H; $CH_3CH_2CH_2$), 1.6–1.75 (m, 2H; CH_2CH_2CH), 4.87 (td, $J =$ 6.2 Hz, $J =$ 1.9 Hz, 1H; CH_2CHOC=O), 6.24 (d, $J = 1.9$ Hz, 1H; CHC*H*=COSi); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 4.82$ (Si(CH_3)$_2$), 13.88 (H_3CCH_2), 18.32 (SiC(CH_3)$_3$), 22.45 (H_3CCH_2), 25.49 (SiC(CH_3)$_3$), 26.82 ($H_3CCH_2CH_2$), 34.02 ($CH_2CH_2CH_2$), 77.98 (O*C*HCH=C), 124.84 (CH*C*H=CO), 142.66 (*C*OSi), 169.49 (C=O); MS (70 eV, EI): *m/z* (%) = 270 (0.92) [M^+], 213 (67), 169 (15), 157 (100), 75 (21); IR (film): $\tilde{\nu} = 2930$, 1757, 1647, 1261, 1148, 1128, 1030, 849, 787 cm^{-1}; $C_{14}H_{26}O_3Si$ (270.4): calcd C 62.18, H 9.69; found: C 62.40, H 10.03.

(*R*)-(−)-3-*tert*-Butyldimethysilyloxy-5-(2-methylpropyl)-2(5*H*)-furanone ((*R*)-9b): The hydrazone (*S,R*)-**8b** (0.240 g, 0.747 mmol) was treated with ozone and *tert*-butyldimethylsilyl chloride, as described above. After column chromatography, the furanone (*R*)-**9b** was obtained as a colorless crystalline solid (0.20 g, 72%). M.p. 40–41 °C; $[\alpha]_D^{23} = -2$ ($c = 0.98$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.25$ (s, 6H; Si(CH_3)$_2$), 0.97 (s, 9H; SiC(CH_3)$_3$), 1.50 (m, 6H; CH(CH_3)$_2$), 1.88 (sept, $J = 6.7$ Hz, 1H; C*H*(CH_3)$_2$), 4.92 (td, $J = 6.7$ Hz, $J = 2.1$ Hz, 1H; C*H*OC=O), 6.23 (d, $J =$ 2.1 Hz, 1H; CHC*H*=COSi); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.82$ (Si(CH_3)$_2$), 18.32 (SiC(CH_3)$_3$), 22.23 (CH(CH_3)$_2$), 23.09 (CH(CH_3)$_2$), 25.00 (*C*H(CH_3)$_2$), 25.48 (SiC(CH_3)$_3$), 43.60 (OCHCH_2CH), 76.65 (O*C*HCH=C), 125.19 (CH*C*H=CO), 142.49 (*C*OSi), 169.45 (C=O); MS (70 eV, EI): *m/z* (%) = 213 (19), 157 (100), 73 (15), 75 (26), 41 (21); IR (film): $\tilde{\nu} = 2850$, 1762, 1651, 1261, 1142, 1129, 890, 856, 844, 758 cm^{-1}; $C_{14}H_{26}O_3Si$ (270.4): calcd C 62.18, H 9.69; found: C 62.16, H 9.81.

(*S*)-(3)-*tert*-Butyldimethysilyloxy-5-(4-methylphenyl)-2(5*H*)-furanone ((*S*)-9c): The hydrazone (*S,S*)-**8c** (0.21 g, 0.61 mmol) was treated with ozone and *tert*-butyldimethylsilyl chloride, as described above. After column chromatography, the furanone (*S*)-**9c** was obtained as a colorless crystalline solid (0.15 g, 81%). M.p. 68–69 °C; $[\alpha]_D^{23} = -31.6$ ($c = 1.04$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.27$ (s, 6H; Si(CH_3)$_2$), 0.98 (s, 9H; SiC(CH_3)$_3$), 2.35 (s, 3H; H_3CAr), 5.81 (d, $J =$ 1.9 Hz, 1H; ArC*H*-OC=O), 6.30 (d, $J = 1.9$ Hz, 1H; CHC*H*=COSi), 7.16 (d, $J = 8.5$ Hz, 2H; 2 arom *m*-CH), 7.17 (d, $J = 8.5$ Hz, 2H; 2 arom *o*-CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.77$ (Si(CH_3)$_2$), 18.34 (SiC(CH_3)$_3$), 21.22 (H_3CAr), 25.49 (SiC(CH_3)$_3$), 79.10 (O*C*HCH=C), 124.38 (CH*C*H=CO), 126.74 (2 arom *m*-CH), 129.57 (2 arom *o*-CH), 132.74 (H_3CAr), 137.38 (arom C), 139.22 (arom C), 142.59 (*C*OSi), 169.48 (C=O); MS (70 eV, EI): *m/z* (%) = 303 (1) [M^+], 247 (100), 203 (69), 129 (39), 75 (28); IR (film): $\tilde{\nu} = 2950$, 1774, 1646, 1254, 1064, 820 cm^{-1}; $C_{17}H_{24}O_3Si$ (303.5): calcd C 67.06, H 7.95; found C 67.36, H 8.10.

(*S*)-(−)-3-*tert*-Butyldimethysilyloxy-5-phenyl-2(5*H*)-furanone ((*S*)-9d): The hydrazone (*S,S*)-**8d** (0.41 g, 1.20 mmol) was treated with ozone and *tert*-butyldimethylsilyl chloride, as described above. After column chromatography, the furanone (*S*)-**9d** was obtained as a colorless crystalline solid (0.20 g, 72%). M.p. 61.5–62.5 °C; *ee* = 98.4% (GC: column 7-CD permethylated, 25 m *T* profile 100-10-198); $[\alpha]_D^{23} = -38.4$ ($c = 0.91$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.27$, 0.28 (s, 6H; 2SiCH_3), 0.98 (s, 9H; SiC(CH_3)$_3$), 5.83 (d, $J =$ 2.2 Hz, 1H; PhC*H*OC=O), 6.33 (d, $J = 2.2$ Hz, 1H; CHC*H*=COSi), 7.26–7.29 (m, 2H; 2 arom o-CH), 7.34–7.38 (m, 3H; 3 arom *m*/*p*-CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.79$ (Si(CH_3)$_2$), 18.30 (SiC(CH_3)$_3$), 25.46 (SiC(CH_3)$_3$), 79.10 (O*C*HCH=C), 124.39 (CH*C*H=CO), 126.67 (2 arom *o*-CH), 128.89 (2 arom *m*-CH), 129.17 (arom *p*-CH), 135.79 (arom C), 142.52 (*C*OSi), 169.38 (C=O); MS (70 eV, EI): *m/z* (%) = 275 (1.97), 233 (100), 189 (76), 115 (56), 103 (25), 75 (31), 59 (11); IR (film): $\tilde{\nu} =$ 3102, 2860, 1769, 1649, 1361, 1287, 1261, 1243, 1133, 1054, 972, 874, 848, 790 cm^{-1}; $C_{16}H_{22}O_3Si$ (290.4): C 66.16, H 7.64; found: C 66.13, H 7.75.

(*S,R*)-(−)-3-*tert*-Butyldimethysilyloxy-5-*O*-cyclohexylidenedioxyethyl-2-(5*H*)-furanone ((*S,R*)-9e): The hydrazone (*S,S,R*)-**8e** (0.42 g, 1.02 mmol) was treated with ozone and *tert*-butyldimethylsilyl chloride, as described above. After column chromatography, the furanone (*S,S,R*)-**9e** was obtained as a colorless oil (0.24 g, 77%); $[\alpha]_D^{23} = -47.5$ ($c = 0.94$, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.23$ (s, 6H; Si(CH_3)$_2$), 0.94 (s, 9H; SiC(CH_3)$_3$), 1.32–1.64 (m, 10H; 5CH_2 (*c*-hexyl)), 3.82–3.84 (m, 1H; OCH_2C*H*O), 4.01 (dd, $J = 9$ Hz, $J = 4$ Hz, 1H; OCH_2CHO), 4.08 (dd, $J =$ 9 Hz, $J = 6$ Hz, 1H; OCH_2CHO), 4.66 (dd, $J = 8$ Hz, $J = 2.1$ Hz, 1H; C*H*OC=O), 6.35 (d, $J = 2.1$ Hz, 1H; CHC*H*=COSi); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -4.82$, 4.79 (Si(CH_3)$_2$), 18.26 (SiC(CH_3)$_3$), 23.69 (CH_2 (*c*-hexyl)), 24.00 (CH_2 (*c*-hexyl)), 25.02 (CH_2 (*c*-hexyl)), 25.43 (SiC(CH_3)$_3$), 34.41 (CH_2 (*c*-hexyl)), 36.53 (CH_2 (*c*-hexyl)), 66.35 (O*C*H$_2$CHO), 76.79 (OCH$_2$*C*HO), 77.83 (O*C*HCH=C), 110.84 (O*C*O), 122.91 (CH*C*H=CO), 143.51 (*C*OSi), 168.88 (s, C=O); MS (70 eV, EI): m/z (%) = 354 (0.92) [M^+], 311 (17), 297 (16), 199 (91), 155 (81), 141 (100), 127 (18), 75 (33), 55 (16); IR (film): $\tilde{\nu} = 2973$, 1769, 1650, 1472, 1385, 1367, 1285, 1244, 1167, 1122, 847, 789 cm^{-1}; $C_{18}H_{30}O_5Si$ (354.5): calcd C 60.98, H 8.53; found: C 61.16, H 8.43.

(*R*)-(−)-3-*tert*-Butyldimethysilyloxy-4-methyl-5-(4-methylphenyl)-2(5*H*)-furanone ((*R*)-9f): The hydrazone (*S,S,S*)-**8f** (0.20 g, 0.53 mmol) was treated with ozone and *tert*-butyldimethylsilyl chloride, as described above. After column chromatography, the furanone (*R*)-**9f** was obtained as a colorless oil (0.11 g, 65%); *ee* > 95% (^{1}H NMR Pirkle shift experiment); $[\alpha]_D^{23} = -88.8$ ($c = 0.97$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.29$ (s, 6H; Si(CH_3)$_2$), 1.00 (s, 9H; SiC(CH_3)$_3$), 1.72 (s, 3H; H_3CC=CO), 2.35 (s, 3H, CH_3Ar), 5.56 (s, 1H; ArC*H*OC=O), 7.10, 7.19 (d, $J = 7.94$ Hz, 4H; Ar); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -3.71$, −3.67 (Si(CH_3)$_2$), 10.62 (H_3CC=CO), 18.81 (SiC(CH_3)$_3$), 21.80 (H_3CAr), 26.17 (SiC(CH_3)$_3$), 82.75 (O*C*HCH=C), 127.54 (2 arom *m*-CH), 130.20 (2 arom *o*-CH), 132.73 (H_3CAr), 138.38 (H_3CC=CO), 138.64 (arom C), 139.84 (*C*OSi), 170.28 (C=O); MS (70 eV, EI): *m/z* (%) = 261 (37), 217 (100), 143 (96), 128 (13), 115 (10), 91 (11)75 (32), 59 (17); IR (film): $\tilde{\nu} = 2930$, 1767, 1687, 1464, 1393, 1341, 1253, 1222, 1138, 888, 843, 821, 788 cm^{-1}; $C_{18}H_{26}O_3Si$ (318.5): calcd C 67.88, H 8.23; found: C 67.89, H 8.23.

(*R*)-3-*tert*-Butyldimethysilyloxy-5-(4-methylphenyl)-4-phenyl-2(5*H*)-furanone ((*R*)-9g): The hydrazone (*S,S,S*)-/(*S,R,S*)-**8g** (0.35 g, 0.80 mmol) was treated with ozone and *tert*-butyldimethylsilyl chloride, as described above. After column chromatography, the furanone (*S*)-**9d** was obtained as a colorless crystalline solid (0.20 g, 65%). M.p. 128–130 °C; *ee* > 98% (^{1}H NMR Pirkle shift experiment); $[\alpha]_D^{23} = -43.3$ ($c = 1.04$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.30$, 0.39 (s, 6H; Si(CH_3)$_2$), 1.01 (s, 9H; SiC(CH_3)$_3$), 2.32 (s, 3H; PhCH_3), 6.15 (s, 1H; ArC*H*OC=O), 7.15, 7.21 (d, $J = 7.7$ Hz, 4H; arom *o*/*m*-CH (*p*MePh)), 7.20–7.30 (m, 3H; 3 arom *m*/*p*-CH (Ph)), 7.26 (d, $J = 8.2$ Hz, 2H; 2 arom *o*-CH (Ph)); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -3.35$, −3.18 (Si(CH_3)$_2$), 19.05 (SiC(CH_3)$_3$), 21.84 (PhCH_3), 26.34 (SiC(CH_3)$_3$), 81.15 (O*C*HCPh=C), 128.34 (2 arom *m*-CH (*p*MePh)), 128.98 (2 arom *o*-CH (*p*MePh)), 129.58 (arom *p*-CH (Ph)), 130.28 (2 arom *o*-CH (Ph)), 130.86 (arom *C*-CH_3), 133.47 (H_3CC=CO), 135.06 (arom C (Ph)), 138.84 (arom C (*p*MePh)), 140.03 (*C*OSi), 169.84 (C=O); MS (70 eV, EI): *m/z* (%) = 379 (0.24([M^+], 323 (52), 279 (100), 263 (5), 205 (32), 193 (4), 178 (8), 91 (4), 75 (17), 59 (9); IR (film): $\tilde{\nu} = 2954$, 1743, 1649, 1464, 1373, 1252, 1167, 1091, 902, 874, 847, 764 cm^{-1}; $C_{23}H_{27}O_3Si$ (379.6): calcd C 2.78, H 7.17; found C 72.77, H 7.34.

(*R*)-3-*tert*-Butyldimethysilyloxy-5-(2-methylpropyl)-4-phenyl-2(5*H*)-furanone ((*R*)-9h): The hydrazone (*S,R,R*)-/(*S,S,R*)-**8h** (80 mg, 0.2 mmol) was treated with ozone and *tert*-butyldimethylsilyl chloride, as described above. After column chromatography, the furanone (*R*)-**9h** was obtained as a colorless oil (50 mg, 72%); $[\alpha]_D^{23} = -36.8$ ($c = 0.95$, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.18$, 0.36 (s, 6H; Si(CH_3)$_2$), 0.74 (d, $J = 6.6$ Hz, 3H; CHCH_3), 0.78 (s, 9H; SiC(CH_3)$_3$), 0.86 (d, $J = 6.6$ Hz, 3H; CHCH_3), 1.38 (ddd, 1H, $J = 14.56$ Hz, $J = 10.44$ Hz, $J = 3.03$ Hz; CHCH_2) 1.67 (ddd, 1H, $J = 14.56$ Hz, $J = 9.62$ Hz, $J = 2.2$ Hz; CHCH_2), 1.96–2.10 (m, 1H; C*H*CH$_2$), 5.36 (dd, 1H; $J = 10.44$ Hz, $J = 2.2$ Hz; CH$_2$C*H*OC=O), 7.34–7.46 (m, 3H; 3 arom *m*/*p*-CH), 7.58 (d, $J = 8.2$ Hz, 2H; 2 arom *o*-CH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = -3.62$, −3.21 (Si(CH_3)$_2$), 18.93 (SiC(CH_3)$_3$), 22.15, 24.09 (CH(CH_3)$_2$), 26.27 (SiC(CH_3)$_3$), 44.16 (CHCH$_2$), 77.79 (O*C*HCPh=C), 128.07 (2 arom *o*-CH), 129.20 (2 arom *m*-CH), 129.61 (arom *p*-CH), 130.96 (H_3CC=CO), 137.55 (arom C), 137.62 (*C*OSi), 170.05 (C=O); MS (70 eV, EI): *m/z* (%) = 347 (0.03) [M^++1], 289 (36), 275 (2), 249 (2), 233 (100), 147 (13), 131 (8), 105 (45), 77 (11), 75 (10); IR (film): $\tilde{\nu} =$ 2957, 1763, 1650, 1470, 1375, 1255, 1169, 1089, 908, 845, 764 cm^{-1}; $C_{20}H_{30}O_3Si$ (346.5): calcd C 69.32, H 8.73; found: C 69.77, H 9.20.

(*S,R*)-(+)-1-[3-*O*-Benzyloxymethyl-3-hydroxy-5-methyl-1-(2,6-di-*tert*-butyl-4-methoxyphenoxycarbonyl)-1-hexylideneamino]-2-(1-ethyl-1-methoxypropyl)pyrrolidine ((*S,R*)-10b): To a solution of (*S,R*)-(0.49 g, 0.87 mmol)

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in anhydrous CH_2Cl_2 (5 mL) was added iPr$_2$NEt (0.45 g, 3.5 mmol), benzylchloromethyl ether (0.41 g, 2.6 mmol), and n-tetrabutylammonium iodide (73 mg, 0.1 mmol) and the mixture was refluxed for 15 h. Methanol (2 mL) was added and the solution was stirred for another 2 h. The solvent was evaporated and the residue dissolved in ether (150 mL). The solution was washed with saturated NaCl solution and dried with $MgSO_4$. After evaporation of the solvent, the product was isolated by column chromatography (silica gel, petroleum ether/ethyl acetate 4:1). (*S*,*R*)-**10b** was obtained as a highly viscous yellow oil which solidified on standing (0.54 g, 93 %). M.p. 57–59 °C. Single crystals for the X-ray structure analysis were obtained by crystallization from methanol at 2 °C. $[\alpha]_D^{23} = +359.0$ ($c = 1$, $CHCl_3$); $de > 98$ % (^{1}H and ^{13}C NMR); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta =$ 0.80–0.93 (d, t, 12H; 2CH$_2$CH_3, CH(CH_3)$_2$), 1.19–2.10 (complex, 11H; 2CH_2CH$_3$, (CH_2CH(CH$_3$)$_2$, NCH$_2$CH_2CH_2), 1.31, 1.36 (2s, 2 × 9H; 2C(CH_3)$_3$), 2.73 (dd, $J = 14.9$ Hz, $J = 4.3$ Hz; 1H, CHHC=N), 2.85 (m, 1H; OH), 2.65 (dd, $J = 7.4$ Hz, $J = 13.8$ Hz, 1H; CHHC=N), 3.10 (dd, J = 6.0 Hz, 13.8 Hz, 1H; CHHC=N), 3.26 (s, 3H; OCH$_3$), 3.45, 3.70, 3.95 (m, 3 × 1H; NCH, NCH_2), 4.15 (m, 1H; CHOCH$_2$), 4.50–4.90 (complex, 4H; OCH$_2$OCH$_2$C$_6$H$_5$), 6.86 (m, 2H; 2arom H), 7.30 (m, 5H; C$_6$H$_5$); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 7.94$, 8.25 (2C(CH$_2$CH_3)$_2$), 21.99, 23.56 (CH(CH_3)$_2$), 23.63 (NCHCH$_2$), 23.85, 25.26 (2C(CH_2CH$_3$)$_2$), 26.95 (NCH$_2$CH_2), 31.10, 31.71 (2C(CH_3)$_3$), 35.57, 35.75 (2C(CH$_3$)$_3$), 36.24 (CH_2C=N), 45.42 (CH_2CH(CH$_3$)$_2$), 50.46 (OCH$_3$), 55.17 (ArOCH_3), 56.38 (NCH$_2$), 69.62 (CH_2C$_6$H$_5$), 73.02 (NCH), 74.92 (CHOCH$_2$), 80.36 (COCH$_3$), 94.30 (OCH$_2$O), 111.44, 111.52 (2arom CH), 127.38 (arom p-CH (Ph)), 128.23 (2arom m-CH (Ph)), 130.80 (CO_2Ar), 138.12 (arom C–CH$_2$), 142.39 (arom C–OCO), 143.60, 143.62 (2arom C–C(CH$_3$)$_3$), 155.99 (arom C–OCH$_3$), 167.21 (C=N); IR ($CHCl_3$): $\tilde{\nu} = 3090$, 3065, 2959, 2880, 1713, 1589, 1566, 1497, 1455, 1420, 1304, 1280, 1251, 1218, 1186, 1169, 1125, 1106, 1069, 1040, 1028 cm^{-1}; $C_{41}H_{64}N_2O_6$ (681.0): calcd C 72.32, H 9.47, N 4.11; found C 72.26, H 9.41, N 4.07.

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[15] Suitable crystals for X-ray analysis were obtained by crystallization from methanol at 2 °C. Monoclinic; space group $P2_1(4)$; $a = 10.940(1)$, $b = 15.822(2)$, $c = 23.817(4)$ Å; $\beta = 92.42(1)^\circ$. From the cell volume of 4118.9 Å^3, two independent molecules in the asymmetric unit, and $M_r = 680.98$ a density of $\rho_{calc} = 1.098\ g\,cm^{-3}$ can be calculated. Total electron count per unit cell $F(000) = 1.488$. Enraf–Nonius CAD4 four-circle diffractometer, graphite monochromator, $\Omega/2\theta$ scans, -50 °C, $Cu_{K\alpha}$ irradiation ($\lambda = 1.54179$ Å), $\mu = 5.42\ cm^{-1}$. A total of 7218 independent reflections ($+h, +k, +l$), of which 6518 were observed. The structure solution was obtained by direct methods (SHELXS-86)[16] and the refinement performed by application of the routines of the SDP program package.[17] The two independent molecules differ considerably in the conformation of the substituents at $C3_{A,B}$ of the five-membered ring. For the phenyl groups $C12_{A,B}$–$C17_{A,B}$, the ideal positions were calculated because of disorder in the atoms $C14_{A,B}$–$C16_{A,B}$ and the substituents refined isotropically as rigid groups. Hydrogen atoms were calculated. For the refinement 783 parameters were used, $R = 0.089$ ($R_w = 0.120$). Isotropic extinction coefficient $a = 2.2 \times 10^{-6}$. Residual electron density is largely localized in the region of the phenyl groups $C12_{A,B}$–$C17_{A,B}$, maximum value: 0.45 e Å^{-3}. Further details of the crystal structure investigation may be obtained from the Fachinformationszentrum Karlsruhe, D-76344 Eggenstein-Leopoldshafen (Germany), on quoting the depository number CSD-56869.

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